Editor's Note: This online data supplement contains supplemental material that was not included with the published article by Richard M. Scheffler and colleagues, "The Global Market for ADHD Medications," *Health Affairs* 26, no. 2 (2007): 450-457(10.1377/hlthaff.26.2.450)

The Global Market for ADHD Medications-Supplemental Exhibits

Richard M. Scheffler, PhD, Stephen P. Hinshaw, PhD, Sepideh Modrek, BA, Peter Levine, MD

Richard M. Scheffler, PhD (corresponding author)
Director, The Nicholas C. Petris Center on Health Care Markets and Consumer Welfare; Distinguished Professor of Health Economics and Public Policy
University of California, Berkeley
2150 Shattuck Avenue, Suite 525
Berkeley, CA 94704
Ph. 510.643.4100; Fx. 510.643.4281; rscheff@berkeley.edu

Stephen P. Hinshaw, PhD
Professor and Chair, Department of Psychology
University of California, Berkeley
3409 Tolman Hall
Berkeley, CA 94720-1650
Ph. 510.643.8586; Fx. 510.642.5293; hinshaw@berkeley.edu

Sepideh Modrek, BA
Agency for Healthcare Research and Quality Pre-Doctoral Fellow; Health Services and Policy Analysis PhD Student
University of California, Berkeley
2150 Shattuck Avenue, Suite 525
Berkeley, CA 94704
Ph. 510.643.4100; Fx. 510.643.4281; smodrek@berkeley.edu

Peter Levine, MD
Department of Pediatrics, Kaiser Permanente
Walnut Creek Medical Center
1425 South Main Street, Medical Office Building, 4th Floor
Walnut Creek, CA 94596
Ph. 925.295.5159; Fx. 925.295.4408; Peter.Levine@kp.org

Date of Submission: 14 February 2007

This study was funded in part by a grant from the National Institute of Mental Health (1R01 MH067084-01 MH1 SRV-C (01)), in part by a grant from The Center for Child and Youth Policy, University of California, Berkeley, and in part by The Nicholas C. Petris Center on Health Care Markets and Consumer Welfare, School of Public Health, University of California, Berkeley.

Overall Findings

Attention deficit hyperactivity disorder (ADHD) is one of the most prevalent childhood disorders in the world, but little is known about the global use and cost of medications used to treat ADHD. Analysis of the IMS Health MIDAS™ database revealed that global utilization of ADHD medications rose three-fold from 1993 through 2003, whereas global expenditures ($2.4 billion U.S. dollars in 2003) rose nine-fold, adjusting for inflation. We also found that per-capita gross domestic product (GDP) robustly predicted utilization for those aged 5-19 years across countries. We present our data, regression methods, and supplemental tables in this appendix.

A. Data

Source

We use the IMS Health MIDAS™ database to analyze trends in the global market for ADHD medications from 1993-2003. IMS Health collects global drug information and receives data from more than 29,000 data suppliers, covering 225,000 data sites around the world.

Medication Categorizations

We classify ADHD medications as those in the ATC=N6B Psychostimulants category, along with the non-amphetamine-like stimulant modafinil (Provigil™, Cephalon) and the non-stimulant atomoxetine HCL (Strattera™, Lilly). Each medication (name brand and generic) was classified into one of four categories, along the dimensions of (a) stimulant versus non-stimulant medications and (b) long-acting (formulations that remain active for at least 8 hours) versus short-acting (fewer than 8 hours). We further classified stimulants by active pharmacologic agent: methylphenidate, amphetamine, or other stimulant. To analyze changes in medication mix, we then generated a three-level categorization of (a) short–acting stimulants, (b) long-acting medications that received FDA approval during the study period, and (c) other long-acting medications. Exhibit A-1 shows the grouping for each major ADHD medication using the categorization described above.

Exhibit A-1: ADHD Medication Categorizations

	Stimulants			Non-stimulants
	Methylphenidates	Amphetamines	Other Stimulants	
Short-acting medications (fewer than 8 hours)	Ritalin Methylin methylphenidate Ritalin SR Methylin ER Metadate ER Focalin	dextroamphetamine Dexedrine Desoxyn mixed amphetamine salts Adderall		
Long-acting medications (8 hours or more)	Ritalin LA Metadate CD Concerta	Dexedrine Spansule Adderall XR	Modafinil Provigil pemoline Cylert	atomoxetine Strattera

Source: The authors

Note: Medications in blue represent those categorized as short-acting medications. Medications in red represent those categorized as long-acting medications, which were approved by the FDA after January 1993. Medications in green represent other long-acting medications.

Dose Measure

As a proxy for dose, IMS Health calibrated each product form into a common metric known as a standard unit (SU). For example, one standard unit could be equivalent to a 5 mg tablet, 5 ml of a liquid, or one injectable vial. Because this measure does not equate medications across active milligrams or molecules of the pharmacological agent, we further adjusted the raw SU to generate dosage equivalence between short-acting and long-acting medications. Given that long-acting medications are generally used once a day whereas short-acting medications require dosing two to three times a day, we weighted the SU of long-acting medications two-fold to correspond to the SU of short-acting agents. We attempted other weighting methods in which individual medications were weighted differently. We found, however, that all of the weighting methods produce similar overall patterns, so we only present the results of the weighting method described above.

Data Inclusion Criteria

In order to be as inclusive as possible, we include all countries that received at least 1,000 SU in a given year and were still receiving at least 1,000 SU in 2003, with no more than 2 consecutive years of use that involved fewer than 1,000 SU. We do this to ensure that we capture as many countries as possible in our analysis. We aggregate data from individual countries from the year that they adopted the use of these medications into a global sum for Exhibits 2, 4, and 5 (see main article).

Utilization

To compare each country's utilization, we used population data from the World Bank and the U.S. Census Bureau to construct a per capita measure. Because ADHD medications were largely prescribed to children and adolescents before 2004(Medco Health Solutions, "ADHD Medication Use Growing Faster among Adults than Children New Research," 2005,www.medco.com, 1 November 2005), our per capita measure was defined as SU divided by the population aged 5-19 years in each country, each year. Note that we use the terms "usage" and "volume" interchangeably throughout the paper. In effect, we assume that medications that reach the country are used within that year.

Expenditure

In the expenditure analysis, U.S. dollars were deflated to 2003 real dollars using the U.S. Consumer Price Index obtained from the U.S. Department of Labor, Bureau of Labor Statistics. Local currency was converted to U.S. dollars by IMS Health using the purchasing power parity (PPP) method. The PPP method considers a bundle of goods and calculates the price of this bundle in each country using local currency. The exchange rate between two currencies is calculated as the ratio of these prices.

B. Regression Methods

Explanation of Regression Analysis

The purpose of our regression analysis was to estimate the independent effect of per capita GDP on the utilization (measured as SU per child aged 5-19) of ADHD medications. Using the panel structure of our data set, we estimated this effect with a fixed-effect model that controlled for country-specific effects and time trends. Fixed-effects estimation is a method of estimating parameters from a panel data set. The fixed-effects estimator is obtained by conducting an ordinary least squares regression on the deviations from the means of each unit and/or time period. This approach is relevant when one expects that the averages of the dependent variable (usage) will be different for each cross-section unit (country) and/or each time period, but the variance of the errors will not. The equations below show the specifications we tested. The predicted values from specification (3) were used in Exhibit 3 (see main article). Exhibit B-1 shows regression estimates for all three specifications.

$$(1)\ (\text{Usage per child aged 5-19})_{it} = b_0 + b_1(\text{GDP/cap})_{it} + \varepsilon_{it},$$

$$(2)\ (\text{Usage per child aged 5-19})_{it} = b_0 + b_1(\text{GDP/cap})_{it} + b_2\,(\text{Country})_i + \varepsilon_{it},$$

$$(3)\ (\text{Usage per child aged 5-19})_{it} = b_0 + b_1(\text{GDP/cap})_{it} + b_2\,(\text{Country})_i + b_3(\text{Time})_t + \varepsilon_{it},$$

In the above specifications, i denotes country, t denotes time, and ε_{it} is the error term. We used all the observations from the OECD countries to estimate the relationship above, but we only plot observations for countries with over 1000 SU in 2003 in Exhibit 3.

The F statistic indicates that our overall model was significant at 0.001 level. The R-squared shows that specification (3) explains 42% of the variation in the dependent variable.

Using a log-log version of our final model, we find that a 1% change in per capita GDP leads to a 3.2% increase in utilization.

Exhibit B-1: Estimated Coefficients for the Relationship between Gross Domestic Product per Capita and Utilization of ADHD Medication per Child (aged 5-19)

Dependent Variable: SU per child aged 5-19 (OECD sample only)			
Variable	Specification (1) Parameter Estimate	Specification (2) Parameter Estimate	Specification (3) Parameter Estimate
Intercept	-3.673**	-5.702**	-5.000**
(t-stat)	(-4.78)	(-9.04)	(-2.96)
GDP/cap in $1000	0.302**	0.396**	0.385**
(t-stat)	(6.48)	(13.66)	(6.10)
Country Fixed Effect	No	Yes	Yes
Time Fixed Effect	No	No	Yes
F-Test	p<0.005	p<0.001	p<0.001
R-Squared	0.205	0.412	0.422
Observations	294	294	294

**p < 0.005

Source: IMS Health, IMS MIDAS™, 1993-2003

Growth Rates

All growth rate calculations in the paper and in this appendix were calculated using a least squares regression model, $\ln(x_{year}) = \alpha + \beta \times (\text{year})$, where x is the variable of interest (e.g., expenditures), and the average annual growth rate in x is the following: $\exp(\beta)-1$. For more information on this method, see http://web.worldbank.org/WBSITE/EXTERNAL/DATASTATISTICS/0,,contentMDK:20452034~pagePK:64133150~piPK:64133175~theSitePK:239419,00.html.

C. Supplemental Tables

Growth in Per Capita Utilization of ADHD Medications from 1993-2003 for Developed and Developing Countries

To understand the differential use of ADHD medications in both developed and developing countries, we calculated the average annual growth rate of usage (SU per child aged 5-19) since 1999. In this analysis, we only included countries that had more than 1,000 SU of use during 1999-2003. Exhibit C-1 shows developed countries per capita use rate in 1999 and 2003 as well as the four-year annual growth rate. Exhibit C-2 shows these data for developing countries.

Exhibit C-1: Growth in ADHD Medication Utilization from 1999-2003 for Developed Countries*

Country	SU per Child Aged 5-19 1999	SU per Child Aged 5-19 2003	4-Year Annual Growth Rate
New Zealand	6.93	6.60	-1.8%
Czech Republic	0.37	0.40	0.6%
Australia	13.30	14.60	2.3%
Slovenia	0.27	0.38	5.9%
Singapore	0.21	0.28	7.5%
United States	26.80	38.50	10.0%
Canada	11.40	17.10	10.7%
United Kingdom	2.76	4.46	12.3%
Belgium	3.82	6.03	12.3%
Mexico	0.28	0.48	14.0%
France	0.75	1.21	14.5%
Japan	0.92	1.66	15.9%
Germany	2.32	4.60	17.7%
Switzerland	3.15	6.69	17.8%
Israel	1.39	2.99	18.6%
Norway	3.40	8.12	23.0%
Luxembourg	3.19	7.58	23.9%
Korea, South	0.22	0.57	26.2%
Spain	0.82	2.37	30.0%
United Arab Emirates	0.02	0.06	39.7%
Austria	0.24	0.96	41.2%
Greece	0.03	1.23	122.8%

* Countries classified as high income by the World Bank.

Notes: Hong Kong data is not reported because we did not have separate age-specific population data.

For the United States in 2003, the CDC estimated that 4.3% of children aged 4-17 years had been diagnosed with ADHD and were currently taking medication for the disorder (Source: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5434a2.htm). Using this estimate, we find that 895 SU (38.5/0.043) were used per medicated child per year, which equals approximately 2.5 SU per medicated child per day.

Exhibit C-2: Growth in ADHD Medication Utilization from 1999-2003 for Developing Countries**

Country	SU per Child Aged 5-19 1999	SU per Child Aged 5-19 2003	4-Year Annual Growth Rate
Argentina	0.80	0.54	-13.0%
Pakistan	0.03	0.02	-10.6%
Ecuador	0.12	0.10	-5.1%
Saudi Arabia	0.02	0.03	2.9%
Peru	0.03	0.04	3.1%
Uruguay	0.53	0.54	3.6%
Chile	0.25	0.38	7.3%
Venezuela	0.05	0.07	7.6%
South Africa	0.40	0.55	8.7%
Malaysia	0.01	0.01	22.3%
Thailand	0.03	0.07	22.6%
Dominican Republic	0.02	0.05	31.2%
Brazil	0.01	0.19	95.2%

** Countries classified as low or middle income by the World Bank.

Growth in Expenditures on ADHD Medication in Developed and Developing Countries

To understand the variation in expenditures of ADHD medications in both developed and developing countries, we estimated the average annual growth rate of expenditures. Again, we only included countries that had more than 1,000 SU of use during 1999-2003. Exhibits C-3 and C-4 show the level of expenditures for ADHD medications in 1999 and 2003 as well as the four-year annual growth rate for developed and developing countries, respectively.

Exhibit C-3: Growth in ADHD Medication Expenditures from 1999-2003 for Developed Countries*

Country	1999 Expenditure (in thousands 2003$)	2003 Expenditure (in thousands 2003$)	4-Year Annual Growth Rate
Hong Kong	93	81	0.4%
New Zealand	1,458	1,618	4.1%
France	10,724	12,742	6.0%
Australia	5,659	7,948	6.3%
Japan	1,899	2,742	8.2%
Slovenia	9	15	11.1%
Czech Republic	60	99	13.5%
Canada	10,490	19,058	13.8%
Singapore	58	105	15.9%
Korea, South	380	1,048	25.9%
Spain	815	2,161	27.1%
Germany	8,437	24,974	27.5%
United Arab Emirates	1	4	29.8%
United Kingdom	8,076	23,952	30.8%
Mexico	1,790	6,311	35.5%
United States	632,622	2,227,862	39.5%
Switzerland	443	2,096	40.6%
Luxembourg	54	242	42.4%
Belgium	487	2,225	43.4%
Israel	274	1,464	46.8%
Austria	95	619	53.9%
Norway	320	3,238	71.5%
Greece	47	1,831	121.9%

* Countries classified as high income by the World Bank.
Note: Although Hong Kong’s 2003 expenditure is below its 1999 expenditure, the calculated growth rate is positive due to a high interim expenditure value.

Exhibit C-4: Growth in ADHD Medication Expenditures from 1999-2003 for Developing Countries**

Country	1999 Expenditure (in thousands 2003$)	2003 Expenditure (in thousands 2003$)	4-Year Annual Growth Rate
Argentina	1,561	1,219	-12.0%
Pakistan	109	80	-9.2%
Uruguay	74	56	-4.8%
Ecuador	74	61	-2.1%
Saudi Arabia	12	14	2.7%
Venezuela	28	37	3.6%
Chile	417	590	5.9%
Peru	48	90	13.0%
South Africa	1,609	3,778	19.3%
Thailand	59	165	21.8%
Dominican Republic	34	75	24.3%
Malaysia	19	57	32.9%
Brazil	119	1,507	87.8%

** Countries classified as low or middle income by the World Bank.

Sampling of ADHD Medication Prices

In our analysis we found that the increase in expenditures for ADHD medication in the U.S. market, which accounts for most of the global expenditures, was due mostly to price increases of these medications. We present a sampling of prices of these medications from a recent *Consumer Reports Best Buy Drugs* in Exhibit C-5. This exhibit shows a large price differential between short- and long-acting formulations.

Exhibit C-5: ADHD Medication Price Comparison

Generic Name and Dose	Brand Name	Generic	Average Monthly Price	Formulation
Amphetamine mixture CD capsule 5 mg tablet	Adderall XR	No	$124	Long
Atomoxetine 10mg capsule	Strattera	No	$138	Long
Methylphenidate SR 18mg tablet	Concerta	No	$109	Long
Amphetamine mixture 5 mg tablet	Adderall	No	$80-$160	Short
Amphetamine mixture 5 mg tablet	Generic	Yes	$43-$86	Short
Dextroamphetamine 5mg tablet	Dexedrine	No	$18-$36	Short
Dextroamphetamine 5mg tablet	Generic	Yes	$10-$20	Short
Methylphenidate 5mg tablet	Ritalin	No	$45	Short
Methylphenidate 5mg tablet	Generic	Yes	$25	Short

Those medications with blue font represent those categorized as short-acting and those in red font represent those categorized as long-acting medications. This follows our categorization in Exhibit A-1. The listings above include only a sampling of ADHD medications. These average monthly prices reflect the U.S. national average retail price for July 2005. Data adopted from *Consumer Reports Best Buy Drugs*, which analyzed data from NDC Health (source: http://www.crbestbuydrugs.org/PDFs/ADHDFinal.pdf, accessed 11 December 2006).